Towards understanding and reducing late side effects of radiotherapy in breast cancer patients

Valorisation

Relevance

Breast cancer is the most common cancer in women[1]. In the last decades, the incidence of breast cancer has risen. In the Netherlands, over 17.000 women were diagnosed with breast cancer in 2019[2]. At the same time, the treatment of breast cancer patients has improved substantially[1,3], leading to a growing number of breast cancer survivors. Especially in the patient population with a good oncological prognosis, preventing late side effects becomes increasingly important.

In this thesis we mainly focussed on three late side effects, namely cosmetic outcome, as we believe cosmetic outcome is related to quality of life, quality of life in a broader sense and preventing radiation induced heart damage.

We analysed data of the Young Boost Trial regarding cosmetic outcome at 4 years of follow up. We investigated which symmetry features are most important for patients to be satisfied with the appearance of her breast after breast conserving therapy. These findings might be relevant for surgeons, when they need to decide about surgery techniques. Further, we were able to define some radiation related factors and adjuvant chemotherapy as risk factors for worse cosmetic outcome[5]. Having knowledge about the Dose Volume Histogram parameters which are important for deterioration of cosmetic outcome, can be helpful for the radiation oncologist when reviewing the treatment plan. In literature many other risk factors for cosmetic outcome are known. Although there is still a lack in knowledge concerning the order of importance of the different risk factors and with that how to deal with them, we feel that these results can be helpful when informing patients about the risks and benefits of the radiation treatment.

We reported on the step-by-step implementation of a voluntary moderate deep inspiration breath hold technique[6], a simple and inexpensive method to spare the heart in case of left sided breast cancer. It is known that dose to the heart can lead to heart damage, whereby the higher the dose in the heart, the higher the risk of heart disease during follow up. Therefore, it is important to keep the dose in the heart as low as possible. We showed a reproducible and affordable breath hold manoeuvre to reduce the dose to the heart. This paper can be helpful for radiation departments all over the world looking for a method to keep the dose in the heart as low as reasonable possible (ALARA).

At last, we investigated whether patient reported outcome measures (PROMs) are sufficiently reliable to record late outcome[7]. We concluded that it is possible to rely on questionnaires for recording late

side-effects. These findings are very relevant for both breast cancer patients in the follow up as well as for breast cancer patients prior to the start of radiation therapy. By using PROMs, the patient can be saved a visit to the hospital during follow up. During consultation before start radiation therapy, patients can be informed regarding potential late side effects based upon the PROM data collected by the treating radiation therapy department. At last, we found that, although patients scored their toxicity a little higher than reported by the doctor at the outpatient clinic, questionnaires can be used to determine toxicity of treatment at a group level en therefore PROMs can be used for measuring quality of care.

Target groups

Breast cancer patients to be treated with curative intent, are the most important target group of this thesis. They may benefit directly or indirectly from the results obtained in this current thesis. For example, women with early breast cancer, treated with breast conserving therapy, can be better informed about the risk of deteriorated cosmetic outcome, if more is known about the risk factors predicting poor cosmetic outcome. These data, in addition to data collected by PROMs, can be used in the shared decision making conservation with the patient. In addition, by worldwide implementing the relatively simple technique of voluntary moderately deep inspiration breath hold, much less women will experience radiation-induced cardiac injury.

Furthermore, clinicians in the field of breast cancer and radiotherapy are likely to be interested in the results of our study. As a result of increasing attention of the government, health insurance companies and patient organizations for more transparency regarding quality indicators, it is important for all care providers to measure the quality of care. Using PROMs is a reliable method to record late effects of a treatment.

Innovation

Each of the studies in the current thesis has an innovative aspect. The Young Boost Trial is the only study with using a boost dose as high as 26 Gy. Further, the paper regarding the implementation of the voluntary moderate deep inspiration breath hold was the first article reporting on both set-up and in vivo dosimetric data obtained during breath hold, which is another form of innovation. At last, the development and design of the outpatient clinic for late outcome with the specific goal to investigate whether a visit to the hospital can be replaced by questionnaires to determine toxicity of the treatment can also be considered as innovative.

Planning & Realisation

The analysis of the cosmetic outcome in the Young Boost Trial have provided clues regarding the risk of a deteriorated cosmetic outcome. As described in the general discussion, the next step is to develop a nomogram to estimate cosmetic outcome. The results of PROMs will also allow development of prognostic models for other side effects that are considered to be relevant by patients. To find out exactly which late side effects patients consider to be relevant, a continuation of the BRASA study (a study with the aim to implement a decision aid for breast cancer and DCIS patients to decide on their radiation treatment) is currently under development. A workshop will be organized in which patients are asked patients for their opinion concerning relevant late side effects on which they might base their choice of treatment. In addition, patients are asked how this can best be visualized in the decision aid. In the future, these individualised predictions can then be used in shared decision making on radiation treatment.

In the Netherlands, proton therapy has become available for almost two years. Patients with breast cancer are only eligible for this treatment in The Netherlands, when a clinically relevant reduction in the risk of late heart damage can be achieved with proton therapy. For now, this clinically relevant reduction of heart injury is estimated based om a prognostic model. To prove the benefit of proton therapy, it is important to record late toxicity. In the long term, for example, data can be used to demonstrate that proton therapy does indeed reduce the risk of heart damage. Another application of the use of questionnaires / PROMS is, as mentioned above, to get insight in the toxicity of your own patient population. Radiotherapy departments will be able to compare (benchmark) their score on late toxicity with other radiotherapy departments. Departments that perform below average will be motivated to improve and the best performing departments can be asked to share their best practice with the other departments to allow them to improve.

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